

1.B The road to a Pharmaceutical Quality System

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Here you will find answers to the following questions:

- How has the concept of “quality” in the pharmaceutical industry changed over the past decades?

Pharmaceutical quality has been a long time in development. Until the 80th, the predominant philosophy was that **Quality Control (QC)** testing alone could determine the quality of the medicinal (drug) product. This concept had serious limitations. Compared with other industries, where it is feasible to test 100% of products, pharmaceutical testing must rely on representative samples – testing of 100% of pharmaceutical products would leave nothing for the patient to consume! When only samples are tested, serious problems can go undetected. As an example, sterile products on the market have shown microbiological contamination even though the samples were free of microorganisms.

The realization that testing alone could not reliably determine whether a product was meeting its predefined specifications gave rise to the concept of the **Quality Assurance (QA)** partnership. To judge the quality of a pharmaceutical product, it is necessary to have additional information as to how it has been manufactured. This awareness led to the development of measures such as batch record review, investigation reporting and approval of manufacturing documents by the quality department.

The major drawback with the QA concepts that companies implemented was that they were reactive rather than proactive. All activities focused on assessing the status quo and fixing problems as they arose. At this time the pharmaceutical industry was not prepared to take the next step towards an overall *quality concept*, as laid down in **ISO 9001:2000** and associated documents. Compliance with GMP regulations was the main preoccupation, and Health Authority inspections at this time supported this narrow view.

Nevertheless, the growing complexity of the operational environment in the pharmaceutical industry, compounded by the growing size of Pharma concerns meant that it became increasingly difficult to achieve compliance with all aspects of GMP regulations.

The industry began to adopt the term **Quality Management (QM)** and to take stock of a number of GMP topics such as change control, recall management, equipment maintenance, validation, handling of discrepancies, etc. necessary to achieve compliance. Individual systems were developed for specific topics, and these operated independently and side-by-side but were never seen as parts of the bigger picture.

In a Science Board Meeting in November 2001 the FDA raised concerns about the efficiency of the pharmaceutical industry. It was said that greater efficiency would be required to get high quality drugs to market quickly enough to take advantage of the new drug development opportunities offered by advances in chemistry and biology. Additionally, the FDA underlined the need for optimal use of public and private resources to meet growing health care needs while obtaining global competitiveness for the pharmaceutical industry.

In conclusion, the status quo was no longer tenable: pharmaceutical manufacturers could do much better. Furthermore, traditional metrics were said to be hiding poor performance, and compliance “infrastructure” with quality-related costs currently running in excess of 20 percent, was uneconomical.

The agency’s findings showed that too often, processes were not fully understood, and that this was still the case once scaled up for commercial production. This problem, they maintained, was compounded by a lack of scientific basis for deeper process understanding.

In 2004, the FDA introduced its “GMP initiative for the 21st century”. This would bring the pharmaceutical industry to the next level of understanding in terms of quality, with the introduction of **Quality Management Systems (QMS)**. At this point it is disgraceful to note that the pharmaceutical industry was presumably one of the last industries to recognize the benefits of a QMS. Since many years, the QMS concept helped other industries to increase their process robustness and thus bring down the price of quality.

The basic philosophy of this concept for the pharmaceutical industry was finally laid down in the **ICH Q10** document *Pharmaceutical Quality Systems* (2008, see chapter E.10). This document heralded a paradigm change across the industry. We now take a holistic view of the entire organization and embed GMP requirements into the overall system.

This approach will allow the pharmaceutical industry to take the quantum leap from reactive to proactive behavior, to recognize discrepancies and not only fix them, but introduce measures that prevent reoccurrence. As a consequence, the pharmaceutical industry will move into a loop of continual improvement and finally increase the robustness of its processes, in production as well as in business.

A Quality Management System enables a company to implement effective, efficient, transparent and simple processes and structures to achieve continual compliance. In addition, this will benefit the company’s business in terms of improved quality, optimized costs, inspection readiness and customer satisfaction.

Summary

Pharmaceutical organizations became more and more complex over the past decades and thus needed to adapt the concept of “quality” from “Quality Control” to modern approaches like Pharmaceutical Quality Systems as laid down in ICH Q10.